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BRIEF COMMUNICATION

Gingkolide B as migraine preventive treatment in young age: results at 1-year follow-up

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Abstract Primary headaches, migraine and tension-type headaches are some of the most frequent conditions in young age. Even before pharmacological treatment, it is mainly useful in these patients to adopt an appropriate lifestyle, with regular sleep, meals, computer and TV, sport, and avoiding triggers. Any specific and effective pharmacological treatment for migraine and tension-type headache is never lacking in side effects. Gingkolide B, an herbal constituent extract from Ginko biloba tree leaves, is a natural anti platelet activating factor (PAF). PAF is a potent pro inflammatory and nociceptive agent released during the inflammation process. Therefore, Gingkolide B can be considered a promising non pharmacological tool for treatment of migraine with and without aura. In an earlier clinical report, we described our initial attempts to assess the clinical utility of Gingkolide B in a small group of young migraine patients. A small sample of 30 young patients suffering from migraine without aura entered the open-label prospective trial. Migraine without aura was diagnosed according to International Headache Society (IHS) criteria. The treatment was well tolerated and the compliance was good. Despite the uncontrolled open-label design of this study and the small sample of patients, these data show that Gingkolide B seems to be effective as preventive treatment in reducing migraine attack frequency and in attenuating the use of symptomatic medication in our small series of children with primary headache.

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Introduction

Primary headaches, migraine and tension-type headaches are some of the most frequent conditions in young age. Recurrent headaches are common in children and adolescents affecting their quality of life negatively [1], at school and social activities [2]. Even before pharmacological treatment, it is mainly useful in these patients to adopt an appropriate lifestyle, with regular sleep, meals, computer and TV, sport, and avoiding triggers.

Parents of children suffering for migraine attack prefer to limit the assumption of symptomatic medication by adopting non pharmacological treatment, when possible. Any specific and effective pharmacological treatment for migraine and tension-type headache is never lacking in side effects. The same preventive drugs used by adults but at reduced dosage are prescribed to children. Treatment comparisons have been included in some recent pharmacological studies, with encouraging results [3].

One of the non pharmacological treatments for headache and tension-type headache in young patients, magnesium, proved to be successfully used [4].

Gingkolide B, a natural anti platelet activating factor (PAF) is an herbal constituent extract from Ginko biloba tree leaves. PAF has proved to be a strong pro inflammatory and nociceptive agent released during inflammatory process. Moreover, Gingkolide B modulates the action of glutamate acid, the main excitatory neurotransmitter of CNS. Migraine aura and spreading depression can be caused by abnormal levels of glutamate in susceptible individuals and the PAF released from platelets and

leukocytes during the first phase of migraine without aura attacks, sensitizes the trigeminal-vascular endings inducing pain.

In an earlier clinical report, we described our initial attempts to assess the clinical utility of Gingkolide B in a small group of young migraine patients [5].

Recently, some other studies have considered administration of Gingkolide B as preventive treatment in primary headache in young patients [6].

By considering the studies of D'Andrea [7] in adult population and the encouraging results of our preliminary study, we decided to treat a larger group of adolescents with Gingkolide B, to confirm the long-term utility on a group of young patients suffering from migraine without aura.

Patients and methods

For this open-label prospective trial, we enrolled a small sample of 30 young patients suffering from migraine without aura, according to International Headache Society criteria [8]. All patients were recruited at the Headache Center of C. Besta Neurological Institute. Inclusion criteria were: age between 8 and 18 years, initial onset of migraine at least 1 year before and at least four migraine attacks (4 days/headache/month) each of the 3 months prior to the screening. Exclusion criteria were: neurological or psychiatric diseases, neuroleptic or antidepressive medication within 6 months before screening, intake of prophylactic medication for migraine in the 6 months before screening, and medication overuse.

They were treated with a combination of Gingkolide B 80 mg, coenzyme Q10 20 mg, vitamin B2 1.6 mg and magnesium 300 mg in oral administration twice per day, in the morning and in the evening, with meals, for 3 months. Number, duration and severity of migraine attacks and analgesic intake were assessed in a diary card 1 month before the starting of the trial and during the treatment period. After 3 months, all patients were checked with their daily card for number, duration, severity headache episodes and analgesic consumption. Follow-up sessions were planned for 3, 6, and 12 months after screening visit.

Results

A total of 30 patients (18 females and 12 males; mean age was 13.5 ± 2.2) entered the study. Mean duration of illness was 3.4 ± 2.4 years. The mean number of days of headache per month was 8.7 ± 7; the mean number of medications/month was 5.2 ± 4.4.

Twenty-three patients (76.6%) achieved the 12-month follow-up, and seven patients never came to the first treatment appointment. The number of monthly migraine attacks was substantially reduced after 3 months of treatment with Gingkolide B in relation to pre study baseline. Starting with mean baseline of 7.2 ± 4.3 attacks, clinical improvement was significant at 1-year follow-up: the mean number of days of headache per month decreased to 1.6 ± 1.7 (p 0.000), with a decrease of number of analgesics used for the attacks from 5.2 ± 4.7 to 0.8 ± 1.4 (p 0.000).

The treatment was well tolerated and the compliance was good: patients (and parents too) reported substantial improvement of their migraine compared to the situation prior to the study. None of the patients reported worsening of migraine.

Conclusion

Data regarding this small group of children with primary headache confirm that Gingkolide B seems to be effective as preventive treatment in reducing migraine attack frequency and in attenuating the use of symptomatic medication.

It is not yet very clear how Gingkolide B improved migraine in young age and also the mechanism of action of Gingkolide B on the CNS. It is believed that the main therapeutical effect may be due to the modulation and/or reducing the excitatory effect of glutamate in the CNS, and glutamate is involved in spreading depression [9]. Another effect of Gingkolide B is to hinder the pathological action of PAF that during some physiopathological circumstances in CNS sensitizes the trigeminal-vascular endings and induces pain [10].

Despite the uncontrolled open-label design of this study and the small sample of patients, these results indicate that this treatment could be a good option for patients suffering from migraine without aura in particular for young patients where therapies without side effects are needed.

Conflict of interest The authors declare that there is no actual or potential conflict of interest in relation to this article.

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